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Health and Environmental Effects Profile for Chlorthiophos

(U.S.) Environmental Protection Agency
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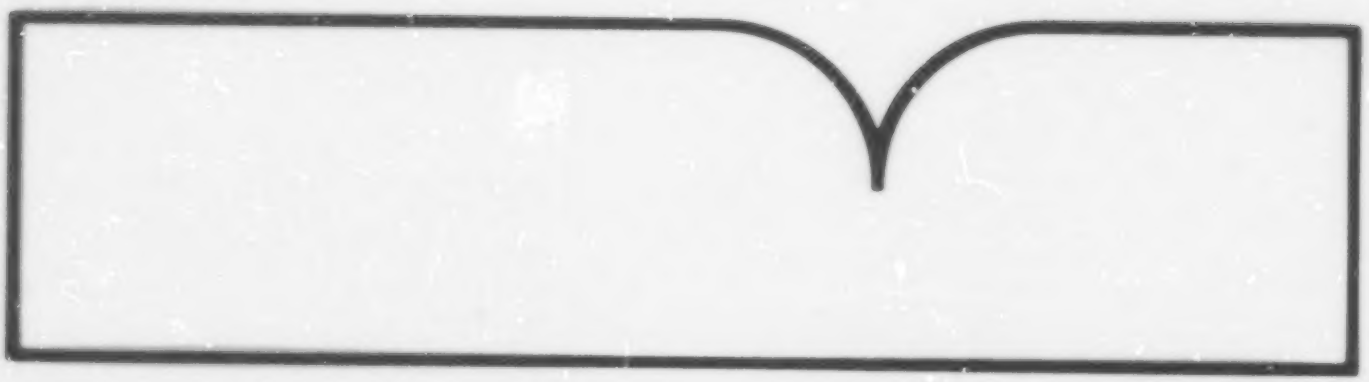

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16. ABSTRACT

The Health and Environmental Effects Profile for Chlorthiophos was prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH for the Office of Solid Waste and Emergency Response to support listings of hazardous constituents of a wide range of waste streams under Section 3001 of the Resource Conservation and Recovery Act (RCRA; and to provide health-related limits for emergency actions under Section 101 of the Comprehensive Environmental Response, Compensation and Liability Act (CERCLA). Both published literature and information obtained from Agency program office files were evaluated as they pertained to potential human health, aquatic life and environmental effects of hazardous waste constituents.

Quantitative estimates have been presented provided sufficient data are available. Chlorthiophos has been determined to be a systemic toxicant. An Acceptable Daily Intake (ADI), defined as the amount of a chemical to which humans can be exposed on a daily basis over an extended period of time (usually a lifetime) without suffering a deleterious effect, for chlorthiophos is 0.8 ug/kg/day for oral exposure.

The Reportable Quantity (RQ) value of 1, 10, 100, 1000 or 5000 pounds is used to determine the quantity of a hazardous substance for which notification is required in the event of a release as specified by CERCLA based on chronic toxicity. Existing data are insufficient to determine an RQ value.

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HEALTH AND ENVIRONMENTAL EFFECTS PROFILE FOR CHLORTHIOPHOS

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This document has been reviewed in accordance with U.S. Environmental Protection Agency policy and approved for publication. Mention of trade names or commercial products does not constitute endorsement or recommendation for use.

PREFACE

Health and Environmental Effects Profiles (HEEPs) are prepared for the Office of Solid Waste by the Office of Health and Environmental Assessment. The HEEPs are intended to support listings of hazardous constituents of a wide range of waste streams under Section 3001 of the Resource Conservation and Recovery Act (RCRA). Both published literature and information obtained from Agency program office files are evaluated as they pertain to potential human health, aquatic life and environmental effects of hazardous waste constit- uents. The literature searched and the dates of the searches are included in the section titled "Appendix: Literature Searched."

Quantitative estimates are presented provided sufficient data are available. For systemic toxicants, these include, Acceptable Daily Intakes (ADIs) for chronic exposures. An ADI is defined as the amount of a chemical to which humans can be exposed on a daily basis over an extended period of time (usually a lifetime) without suffering a deleterious effect. In the case of suspected carcinogens, ADIs are not estimated in this document series. Instead, a carcinogenic potency factor or q_1^* is provided. These potency estimates are derived for both oral and inhalation exposures where possible. In addition, unit risk estimates for air and drinking water are presented based on inhalation and oral data, respectively.

The first draft of this document was prepared by Syracuse Research Corporation under EPA Contract No. 68-03-3228. The document was subsequently revised after reviews by staff within the Office of Health and Environmental Assessment: Carcinogen Assessment Group, Reproductive Effects Assessment Group, Exposure Assessment Group, and the Environmental Criteria and Assessment Office in Cincinnati.

The HEEPs will become part of the EPA RCRA docket.

ACKNOWLEDGEMENTS

The initial draft of this report was prepared by Syracuse Research Corporation under Contract No. 68-03-3228 for U.S. EPA's Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH. Dr. Christopher DeRosa was the Technical Project Monitor and Helen Ball was the Project Officer. The final documents in this series were prepared for the Office of Solid Waste, Washington, DC.

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EXECUTIVE SUMMARY

Chlorthiophos is a mixture of three isomeric compounds in which the isomer O-2,5-dichloro-4-(methylthio)phenyl O,O-diethylphosphorothionate predominates. It is a yellow-brown liquid at temperatures >25°C and is sparingly soluble in water but soluble in most organic solvents. The compound may be slowly oxidized (Iwata et al., 1982) in the air and may undergo slow hydrolysis in water (Worthing and Walker, 1983).

Chlorthiophos is not manufactured in the United States but is imported by E.M. Industries, Inc., Elmsford, NY from its manufacturer Celamerk GMBH and Co., KG, Ingelheim, Germany. It is used as a nonsystemic insecticide against biting, sucking and mining insects, spider mites and mosquito larvae (Meister, 1981). The tolerence level for use of this insecticide on tomato plants is 0.5 ppm (CFR, 1982).

Data regarding the environmental fate and transport of chlorthiophos are limited to estimates derived from its physical and chemical properties and from a study by Iwata et al. (1982). Chlorthiophos is likely to enter the atmosphere through volatilization and suspension of soil dust from treated fields. Chlorthiophos may undergo oxidation reactions in the atmosphere, with an estimated oxidation half-life of <2.7 days. Neither wet nor dry deposition is expected to remove significant amounts of chlorthiophos from the atmosphere.

Three mechanisms that may be responsible for the degradation of chlorthiophos in water are hydrolysis, oxidation and biodegradation. The half-life for hydrolysis is ~42 days (Worthing and Walker, 1983), and no estimations of half-lives for oxidation or biodegradation in water are possible.

The volatilization of chlorthiophos from water is probably slow but is an important transport mechanism. Significant amounts are likely to be present in suspended particles and sediments in water. Bioconcentration in aquatic organisms may be moderate.

The half-life for the oxidation of chlorthiophos in soil surfaces may be ~7 days. Hydrolysis in wet soil may occur. Biodegradation in soil may be significant; however, pertinent data were not available. The significance of volatilization of chlorthiophos from soil cannot be estimated. Significant leaching into groundwater is unlikely. Data regarding exposure to chlorthiophos in air, water or commercial food products were not available. The level of chlorthiophos and its degradation products in the edible portion of oranges was <0.01 ppm at all times after treatment for up to 60 days (Iwata et al., 1982).

Pertinent data regarding the pharmacokinetics and metabolism of chlorthiophos could not be located in the available literature as cited in the Appendix. The available information regarding the toxic effects of exposure to chlorthiophos is limited. No data on the carcinogenicity, mutagenicity or teratogenicity were located. Oral LD_{50} values are 7.8-13 mg/kg for rats, 91.4-141 mg/kg for mice, 20 mg/kg for rabbits and 58 mg/kg for guinea pigs (Worthing and Walker, 1983; Muacevic, 1976; NIOSH, 1985). As an organophosphate insecticide, chlorthiophos inhibits cholinesterase. Dermal treatment with chlorthiophos at 40-160 $\mu g/cm^2$ resulted in 10-60% inhibition of erythrocyte cholinesterase at 72 hours after dosing (Iwata et al., 1982). Maximal inhibition of erythrocyte, plasma and brain cholinesterase activities occurred within 2-6 hours of dosing rats by an unspecified route with an unspecified dose, and returned to normal in 4-8 days (Muacevic, 1976). Dietary exposure of rats to 1.6 ppm (0.08 mg/kg/day) for 2 years and

of dogs to 1 ppm (0.025 mg/kg/day) for 1 year had no effect on erythrocyte cholinesterase activity (Worthing and Walker, 1983). Additional details were not provided. The 96-hour LD_{50} values for bluegills and rainbow trout are 1.3 and 0.019 mg/ℓ, respectively (Worthing and Walker, 1983).

A provisional ADI of 56 µg/day was based on the NOEL of 0.08 mg/kg/day for erythrocyte cholinesterase activity in a 2-year dietary study in rats. The ADI is provisional because sufficient details were not provided to adequately assess the dietary studies. Similarly, data are not sufficient to derive an RQ based on the chronic toxicity of chlorthiophos since toxic levels were not defined. The lack of carcinogenicity data places chlorthiophos in IARC Group 3 and EPA Group D (U.S. EPA, 1984); that is, it cannot be classified as to its carcinogenicity for humans.

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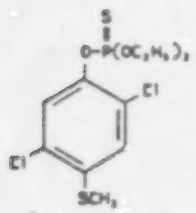
LIST OF ABBREVIATIONS

ADI	Acceptable daily intake
AI	Active ingredient
BCF	Bioconcentration factor
CAS	Chemical Abstract Service
K_{oc}	Soil sorption coefficient standardized with respect to organic carbon
K_{ow}	Octanol/water partition coefficient
LC_{50}	Median lethal concentration
LD_{50}	Median lethal dose
MED	Minimum effective dose
NOEL	No-observed-effect level
ppm	Parts per million
RQ	Reportable quantity
UV	Ultraviolet

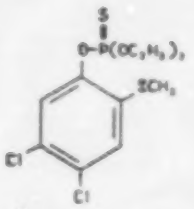
1. INTRODUCTION

1.1. STRUCTURE AND CAS NUMBER

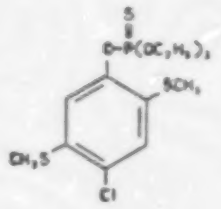
The chemical commonly known as chlorthiophos is a mixture of the following three isomers: (i) O-2,5-dichloro-4-(methylthio)phenyl O,O-diethyl phosphorothionate, (ii) O-4,5-dichloro-2-(methylthio)phenyl O,O-diethyl phosphorothionate and (iii) O-2,4-dichloro-5-(methylthio)phenyl O,O-diethyl phosphorothionate. In commercial chlorthiophos, the main component is isomer (i); isomer (ii) is present in small quantities and isomer (iii) is a minor component (Worthing and Walker, 1983). Some of the trade names of this compound are Celamerk S-2957, Celathion, ENT 27635, NSC 195164, OMS 1342 and S 2957 (NIOSH, 1985). The structure, molecular weight and empirical formula of the three components are as follows:



Isomer (i)



Isomer (ii)



Isomer (iii)

Molecular weight: 361.2

Empirical formula: $C_{11}H_{15}Cl_2O_3PS_2$

The CAS Registry number for the mixed isomer is 60238-56-4 and 21923-23-9 for isomer (i).

1.2. PHYSICAL AND CHEMICAL PROPERTIES

Chlorthiophos is a yellow-brown liquid at temperatures >25°C and is soluble in most organic solvents. Some of the other available physical properties of this compound are given below.

Melting point:	>25°C	Worthing and Walker, 1983
Boiling point:	153-158 at 0.013 mm Hg	Worthing and Walker, 1983
Density at 20°C:	1.345 g/cm³	Worthing and Walker, 1983
Vapor pressure at 25°C:	3.98×10^{-6} mm Hg	Worthing and Walker, 1983
Water solubility at 20°C:	0.3 mg/ℓ (estimated)	Worthing and Walker, 1983
Henry's Law Constant:	6.3×10^{-6} atm·m³/mol	(estimated from vapor pressure and solubility data)
Log K_{ow}:	5.11 (estimated)	Lyman et al., 1982
Log K_{oc}:	3.93 (estimated)	Lyman et al., 1982

Pertinent data regarding the chemical properties of chlorthiophos are limited. These compounds undergo slow hydrolysis in water at pH <9 (Worthing and Walker, 1983) and may also be oxidized in the presence of ozone and UV light (Iwata et al., 1982).

1.3. PRODUCTION DATA

Celamerk GMBH and Co., KG, Ingelheim, Germany manufactures this insecticide (Meister, 1981). Although chlorthiophos is not manufactured in the United States; it is imported by EM Industries, Inc., Elmsford, NY (Iwata et al., 1982). Data regarding the manufacturing process for this insecticide were not available in the literature.

1.4. USE DATA

Chlorthiophos is a nonsystemic insecticide with a broad range of uses against biting, sucking and mining insects, spider mites and mosquito larvae (Meister, 1981). The tolerance level for use on tomato plants has been established at 0.5 ppm by U.S. EPA (CFR, 1982).

1.5. SUMMARY

Chlorthiophos is a mixture of three isomeric compounds in which the isomer O-2,5-dichloro-4-(methylthio)phenyl O,O-diethylphosphorothionate predominates. It is a yellow-brown liquid at temperatures >25°C and is sparingly soluble in water but soluble in most organic solvents. The compound may be slowly oxidized in the air (Iwata et al., 1982) and may undergo slow hydrolysis in water (Worthing and Walker, 1983).

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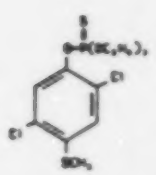
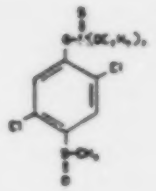
2. ENVIRONMENTAL FATE AND TRANSPORT PROCESSES

2.1. AIR

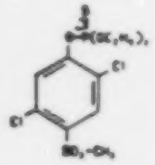
Large gaps exist in the data base on the environmental fate of chlorthiophos in air, water and soil. Therefore, the conclusions reached in this Chapter about the fate and transport of this insecticide are mostly estimates and lack experimental evidence in most instances. Under field application conditions, chlorthiophos oxidizes to the following five products (Iwata et al., 1982):



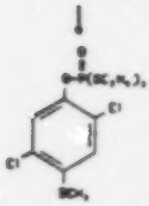
chlorthiophos



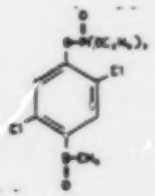
chlorthiophos sulfoxide



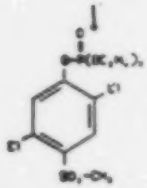
chlorthiophos sulfone



chlorthiophos oxon



chlorthiophos oxon sulfoxide



chlorthiophos oxon sulfone

Chlorthiophos and its five oxidation products were detected in soil dust samples collected from an orange grove after treatment with 9.5 pounds of AI $acre^{-1}$ of the insecticide (Iwata et al., 1982). The concentration of chlorthiophos decreased with almost a first order decay rate from an initial value of ~210 ppm to ~11 ppm in 30 days, resulting in an estimated half-life for this reaction of ~7 days. Oxidation of chlorthiophos ceased after 30 days. The authors speculated that the oxidation was due to the reaction

of ozone and UV light with the insecticide. The lack of oxidation after 30 days may be due to sorption effects of the residual chlorthiophos on the dust. If the half-life of chlorthiophos on soil dust is assumed to be ~7 days, the half-life of the same compound in the vapor phase is expected to be even shorter. In fact, subsequent to spraying the insecticide, the dislodgeable foliar residue level decreased in a first order decay mode from an initial value of 0.8 μg/cm² to 0.005 μg/cm² in ~15 days (Iwata et al., 1982), resulting in a half-life of ~2 days for chlorthiophos not sorbed to the surface of foliage.

The vapor pressure of chlorthiophos is $\sim 3.98 \times 10^{-6}$ mm Hg at 25°C. According to Cupitt (1980), adsorption of vapor to particulate matter in the atmosphere is not expected to be significant unless the vapor pressure is $\leq 10^{-7}$ mm Hg. Therefore, since evaporation of chlorthiophos is likely to occur from treated plants and soils, chlorthiophos is expected to be present in the atmosphere both in the vapor phase and in mobile soil dusts. The oxidation half-life of this insecticide in the atmosphere is expected to range between <2 and 7 days. However, the degradation of chlorthiophos in the atmosphere may not lead to its complete mineralization but to the formation of the other oxidation products already described.

Pertinent data regarding the removal of chlorthiophos from the atmosphere through physical mechanisms could not be located in the available literature as cited in the Appendix. Considering the low aqueous solubility and the expected inability of the vapors of the compound to be sorbed onto atmospheric particles, neither wet precipitation nor dry deposition are likely to be significant compared with its removal through oxidation.

2.2. WATER

Pertinent data regarding the fate and transport of chlorthiophos in water could not be located in the available literature as cited in the Appendix. Based on its physical properties and the studies of Iwata et al. (1982), however, a few speculations can be made regarding the behavior of chlorthiophos in water. The primary source by which this insecticide enters surface waters is likely to be rain water runnoff from soils in treated areas. The two most probable chemical reactions that may degrade chlorthiophos in water are oxidation and hydrolysis. The hydrolysis half-life of this insecticide in water at pH <9 is 42 days, but no other details about the hydrolytic reaction are available (Worthing and Walker, 1983). From the oxidation products detected on sprayed soils, leaves and fruits, Iwata et al. (1982) speculated that this insecticide is oxidized by oxidants and sunlight in the atmosphere. In water, peroxide radicals ($RO\cdot_2$) and other radicals (RO·, HO·) present in most natural aquatic media (Mill et al., 1982) are likely to participate in similar oxidation reactions with this insecticide. The removal rate of chlorthiophos as a result of these reactions cannot be predicted, however, because of the lack of reaction rate data. Biodegradation in water is another probable degradation mechanism for which no data are available.

From the vapor pressure and solubility data (see Section 1.2.) and assuming the water solubility of chlorthiophos at 25°C does not differ appreciably from the value at 20°C, a value of 6.3×10^{-6} atm·m³/mol has been derived for the Henry's Law constant, indicating that although the chlorthiophos volatilization rate from water is slow, it is still a significant transfer mechanism (Lyman et al., 1982). The estimated log K_{oc} value

for chlorthiophos in soil and sediment is 3.93. Therefore, significant amounts of this insecticide are expected to be present in suspended particles and sediments in water.

Pertinent data regarding the possible bioconcentration of chlorthiophos in aquatic organisms could not be located in the available literature as cited in the Appendix; however, the BCFs of a chemical can be estimated from the aqueous solubility using Equation 2-1 (Lyman et al., 1982):

$$\log BCF = 2.791 - 0.564 \log S \qquad (2\text{-}1)$$

Thus, the estimated log BCF for chlorthiophos is 3.09, indicating that moderate bioconcentration may occur.

2.3. SOIL

In the absence of any comprehensive study demonstrating the fate and transport of chlorthiophos in soil, the study by Iwata et al. (1982) has been used to predict some of these characteristics. The estimated half-life for chemical oxidation of chlorthiophos on soil dust samples is ~7 days (see Section 2.1.); therefore, the estimated half-life of the oxidation reaction on the surface of soil where aerobic conditions exist is also ~7 days. Microbial degradation is another mechanism that may be responsible for the significant removal of chlorthiophos from soil; however, no studies on the biodegradation potential for chlorthiophos were located in the available literature. The hydrolysis of chlorthiophos on wet soil is another probable removal mechanism, although the rate of removal by this process is not known.

Chlorthiophos is likely to be removed from soil surfaces by volatilization. Iwata et al. (1982) found ~210 ppm of chlorthiophos on soil dust samples on day 0 following treatment of an orange grove with 9.5 pounds of

AI acre^{-1} of chlorthiophos. Sixty days after treatment, chlorthiophos and its five metabolites accounted for only 52% of the original amount applied, suggesting that chlorthiophos was lost through volatilization, although no quantitative estimate can be made about the the volatilization rate. The estimated log K_{oc} value of 3.93 and low water solubility value suggest that under normal application conditions, chlorthiophos is not likely to leach significantly into groundwater. A reasonable biodegradation rate in soil will further preclude the possibility of leaching into groundwater.

2.4. SUMMARY

Large gaps exist in the data base regarding the environmental fate of chlorthiophos in air, water and soil. Most of the information developed on the fate and transport of the insecticide are estimates, which are based on its physical properties and the extrapolation of data from a single study (Iwata et al., 1982). Chlorthiophos is likely to enter the atmosphere through volatilization and suspension of soil dust from treated fields, and will oxidize in the atmosphere with an estimated oxidation half-life of between <2 and 7 days. Neither wet precipitation nor dry deposition is expected to remove significant amounts of chlorthiophos from the atmosphere.

The three most probable mechanisms responsible for the degradation of this insecticide in water are hydrolysis, oxidation and biodegradation. The half-life for hydrolysis is ~42 days (Worthing and Walker, 1983); the other two reactions may be faster, but no estimations can be made about their half-lives. The volatilization of chlorthiophos from water is expected to be a slow but important transport mechanism. Significant amounts of this insecticide are likely to be present in suspended particles and sediments of aquatic media, but bioconcentration of this insecticide in aquatic organisms may be moderate.

The half-life for oxidation of chlorthiophos on soil surfaces is speculated to be ~7 days. Hydrolysis in wet soils may occur. Biodegradation may be important in degrading chlorthiophos in soil; however, no data were available. The significance of chlorthiophos volatilization from soil cannot be estimated, and it is anticipated that the insecticide will not leach significantly into groundwater.

3. EXPOSURE

Pertinent data regarding residue levels for chlorthiophos in air, water or commercial foods could not be located in the available literature as cited in the Appendix. In one study, an orange grove was treated with 4.8 and 9.5 pounds of AI $acre^{-1}$ of chlorthiophos, and the unwashed orange rind and the pulp were monitored for chlorthiophos and its oxidation products for 60 days (Iwata et al., 1982). The chlorthiophos level on the rind immediately after treatment ranged from 2-5 ppm, but after 60 days, the level on the rind ranged from 0.25-0.6 ppm. The levels of chlorthiophos and its metabolites in the edible portion of the fruit were <0.01 ppm at all times following treatment.

4. PHARMACOKINETICS

Pertinent data regarding the absorption, distribution, metabolism or excretion of chlorthiophos by mammalian species could not be located in the available literature as cited in the Appendix.

5. EFFECTS

5.1. CARCINOGENICITY

Pertinent data regarding the carcinogenicity of chlorthiophos could not be located in the available literature as cited in the Appendix. This chemical is not scheduled for testing by the National Toxicology Program (NTP, 1985).

5.2. MUTAGENICITY

Pertinent data regarding the mutagenicity of chlorthiophos could not be located in the available literature as cited in the Appendix.

5.3. TERATOGENICITY

Pertinent data regarding the teratogenicity of chlorthiophos could not be located in the available literature as cited in the Appendix.

5.4. OTHER REPRODUCTIVE EFFECTS

Pertinent data regarding other reproductive effects of chlorthiophos could not be located in the available literature as cited in the Appendix.

5.5. CHRONIC AND SUBCHRONIC TOXICITY

The only available information regarding the effects of long-term exposure of animals to chlorthiophos was summarized by Worthing and Walker (1983): no effect on erythrocyte cholinesterase activity was observed in rats fed diets containing 1.6 ppm chlorthiophos for 2 years or in dogs fed diets containing 1 ppm chlorthiophos for 1 year. Further details were not provided.

5.6. OTHER RELEVANT INFORMATION

Acute LD_{50} values for chlorthiophos are presented in Table 5-1. Female rats appear to be slightly more sensitive than male rats. Based on oral LD_{50} values, sensitivity to chlorthiophos is as follows: rats > rabbits > guinea pigs > mice. According to Muacevic (1976), the dermal

TABLE 5-1

Acute LD_{50} Values for Chlorthiophos

Route	Species	LD_{50} (mg/kg)	Reference
Oral	rat/male	10.7	Worthing and Walker, 1983
Oral	rat/female	7.8	Worthing and Walker, 1983
Oral	rat	13	Muacevic, 1976
Oral	mouse	91.4	Worthing and Walker, 1983
Oral	mouse	141	Muacevic, 1976; NIOSH, 1985
Oral	rabbit	20	Muacevic, 1976; NIOSH, 1985
Oral	guinea pig	58	Muacevic, 1976; NIOSH, 1985
Dermal	rat/male	153	Worthing and Walker, 1983
Dermal	rat/female	151	Worthing and Walker, 1983
Dermal	rat	58	Muacevic, 1976; NIOSH, 1985
Dermal	rabbit	50-58	Worthing and Walker, 1983
Dermal	rabbit	48	Muacevic, 1976; NIOSH, 1985

LD_{50} values for rats and rabbits are 58 and 48 mg/kg, respectively, while Worthing and Walker (1983) reported values of ~150 mg/kg for rats and 50-58 mg/kg for rabbits.

Dermal treatment of rats with chlorthiophos in acetone at doses of 40, 80 or 160 µg/cm² resulted in 10, 30 or 60%, respectively, inhibition of erythrocyte cholinesterase activity at 72 hours after dosing (Iwata et al., 1982).

As summarized in an abstract of a Russian study (Muacevic, 1976), erythrocyte, plasma and brain cholinesterase inhibition was maximal at 2, 4 and 6 hours, respectively, following treatment of rats with chlorthiophos by an unspecified route at an unspecified dose. Blood and brain cholinesterase levels returned to normal in 4 and 8 days, respectively. Pretreatment of rats with lindane or phenobarbital reduced the toxicity, while pretreatment with atropine, obidoxime chloride or trimedoxime bromide potentiated the toxicity.

5.7. SUMMARY

Pertinent data regarding the carcinogenicity, mutagenicity, teratogenicity or other reproductive effects of chlorthiophos could not be located in the available literature as cited in the Appendix. Oral LD_{50} values are 7.8-13 mg/kg for rats, 91.4-141 mg/kg for mice, 20 mg/kg for rabbits and 58 mg/kg for guinea pigs (Worthing and Walker, 1983; Muacevic, 1976; NIOSH, 1985). As an organophosphate insecticide, chlorthiophos inhibits cholinesterase. Dermal treatment of rats with 40-160 µg/cm² resulted in 10-60% inhibition of erythrocyte cholinesterase activity at 72 hours after dosing (Iwata et al., 1982). Erythrocyte, plasma and brain cholinesterase activities were inhibited maximally at 2, 4 and 6 hours, respectively, after rats were treated with an unspecified dose of chlorthiophos by an unspecified

route; activities returned to normal in 4-8 days (Muacevic, 1976). Worthing and Walker (1983) reported that dietary exposure of rats to 1.6 ppm for 2 years or of dogs to 1 ppm for 1 year had no effect on erythrocyte cholinesterase activity. Additional details were not provided.

6. AQUATIC TOXICITY

6.1. ACUTE TOXICITY

The 96-hour LC_{50} of chlorthiophos for bluegills, Lepomis macrochirus, is 1.3 mg/ℓ, and for rainbow trout, Salmo gairdneri, 0.019 mg/ℓ (Worthing and Walker, 1983).

6.2. CHRONIC TOXICITY

Pertineni data regarding the chronic toxicity of chlorthiophos to aquatic organisms could not be located in the available literature as cited in the Appendix.

6.3. PLANTS

Pertinent data regarding the effects of chlorthiophos on aquatic plants could not be located in the available literature as cited in the Appendix.

6.4. RESIDUES

Pertinent data regarding residues of chlorthiophos in aquatic organsims could not be located in the available literature as cited in the Appendix.

6.5. SUMMARY

Data regarding the aquatic toxicity of chlorthiophos are limited. LD_{50} values of 1.3 and 0.019 mg/ℓ for bluegills and rainbow trout, respectively, were reported by Worthing and Walker (1983).

7. EXISTING GUIDELINES AND STANDARDS

7.1. HUMAN

The tolerance for the combined residues of chlorthiophos and its diethyl phosphorus ester moiety-containing metabolites in or on tomatoes is 0.5 ppm and was promulgated in April, 1981 (CFR, 1982).

7.2. AQUATIC

Guidelines and standards for the protection of aquatic organisms from the toxic effects of chlorthiophos could not be located in the available literature as cited in the Appendix.

8. RISK ASSESSMENT

The available information regarding the toxic effects of exposure to chlorthiophos are limited, and pertinent data regarding the carcinogenicity, mutagenicity or teratogenicity of chlorthiophos were not located in the available literature. Oral LD_{50} values are 7.8-13 mg/kg for rats, 91.4-141 mg/kg for mice, 20 mg/kg for rabbits and 58 mg/kg for guinea pigs (Worthing and Walker, 1983; Muacevic, 1976; NIOSH, 1985). As an organophosphate insecticide, chlorthiophos acts as a cholinesterase inhibitor. Dermal treatment of rats with 40-160 µg/cm² resulted in 10-60% inhibition of erythrocyte cholinesterase activity at 72 hours after dosing (Iwata et al., 1982). Maximal inhibition of erythrocyte, plasma and brain cholinesterase activities occurred at 2, 4 and 6 hours, respectively, after treatment of rats by an unspecified route with an unspecified dose of chlorthiophos (Muacevic, 1976). Activity returned to normal in 4-8 days.

Worthing and Walker (1983) reported that dietary administration of chlorthiophos to rats at 1.6 ppm for 2 years and to dogs at 1 ppm for 1 year produced no effect on erythrocyte cholinesterase. Additional details of the chronic dietary studies were not provided. Assuming that rats and dogs consume a daily amount of food equal to 5% (U.S. EPA, 1980) and 2.5% (Durkin, 1985) of their body weights, respectively, the dietary levels of 1.6 ppm (rat) and 1 ppm (dog) are equivalent to doses of 0.08 mg/kg/day for rats and 0.025 mg/kg/day for dogs. Dividing the higher dose of 0.08 mg/kg/day by an uncertainty factor of 100 (10 for interspecies extrapolation and 10 to protect the most sensitive human individuals) results in a provisional ADI of 0.8 µg/kg/day, or 56 µg/day for a 70 kg man. The ADI must be considered provisional because sufficient details were not provided to adequately

assess the dietary studies. The dietary levels that produced erythrocyte cholinesterase inhibition, which may not be an adverse effect (Wills, 1972), were not reported; furthermore, other endpoints of toxicity were either not examined, not observed or not reported.

9. REPORTABLE QUANTITIES

9.1. REPORTABLE QUANTITIY (RQ) RANKING BASED ON CHRONIC TOXICITY

The only available information regarding the effects of chronic exposure to chlorthiophos was summarized by Worthing and Walker (1983). Chlorthiophos had no effect on erythrocyte cholinesterase activity when administered at dietary levels of 1.6 ppm for 2 years to rats or 1 ppm for 1 year to dogs. Since levels at which effects were observed were not reported, it is not possible to define the MED. Therefore, data are not sufficient for deriving an RQ for chlorthiophos (Table 9-1).

9.2. WEIGHT OF EVIDENCE AND POTENCY FACTOR ($F=1/ED_{10}$) FOR CARCINOGENICITY

Information regarding the carcinogenicity of chlorthiophos was not located in the available literature as cited in Appendix. Therefore, according to the IARC classification scheme, chlorthiophos is a Group 3 chemical. Based on U.S. EPA (1984) guidelines for carcinogen risk assessment and the lack of animal/human cancer data, the compound is classified as Group D, meaning it cannot be classified as to its carcinogenicity for humans.

TABLE 9-1

Chlorthiophos

Minimum Effective Dose (MED) and Reportable Quantitiy (RQ)

Route:

Dose*:

Effect:

Reference:

RV_d:

RV_e:

Composite Score:

RQ: Data are not sufficient for deriving an RQ.

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*Equivalent human dose

10. REFERENCES

Code of Federal Regulations. 1982. Chlorthiophos; tolerances for residues. U.S. EPA. 40 CFR 180.398.

Cupitt, L.T. 1980. Fate of toxic and hazardous materials in the air environment. ESRL, ORD, U.S. EPA, RTP, NC. EPA 600/3-84-084. NTIS PB 80-221948.

Durkin, P.R. 1985. Reference Values for Risk Assessment. Prepared by Syracuse Research Corporation, Syracuse, NY, under Contract No. 68-03-3228. ECAO, U.S. EPA, Cincinnati, OH.

Iwata, Y., J.B. Knaak, G.E. Carman, M.E. Dusch and F.A. Gunther. 1982. Fruit residue data and worker reentry research for chlorthiophos applied to California, USA, citrus trees. J. Agric. Food Chem. 30(2): 215-222.

Lyman, W.J., W.F. Reehl and D.H. Rosenblatt. 1982. Handbook of Chemical Property Estimation Methods. Environmental Behavior of Organic Compounds. McGraw-Hill Book Co., NY. p. 2-14, 4-9, 5-5, 15-16.

Meister, R.T., Ed. 1981. Farm Chemicals Handbook. Meister Publishing Co., Willoughby, OH. p. C77.

Mill, T., W.R. Mahey, D.C. Bomberger, T.-W. Chou, D.G. Hendry and J.H. Smith. 1982. Laboratory protocols for evaluating the fate of organic chemicals in air and water. ESRL, ORD, U.S. EPA, Athens, GA. EPA 600/3-82-022.

Muacevic, G. 1976. Acute toxicity and cholinesterase inhibition *in vivo* of chlorthiophos. Arh. Hig. Rada Toksikol. 27(1): 3-14. (CA 85:104942e)

NIOSH (National Institute for Occupational Safety and Health). 1985. RTECS (Registry of Toxic Effects of Chemical Substances). August, 1985: online.

NTP (National Toxicology Program). 1985. Management Status Report. 8/7/85.

U.S. EPA. 1980. Guidelines and Methodology for the Preparation of Health Effects Assessment Chapters of the Ambient Water Quality Criteria Documents. ECAO, OHEA, ORD, U.S. EPA, Cincinnati, OH. [Also published in Federal Register, 45(231):79347-79357]

U.S. EPA. 1984. Guidelines for Carcinogen Risk Assessment. Federal Register. 49(227): 46294-46301.

Wills, J.H. 1972. The measurement and significance of changes in the cholinesterase activities of erythrocytes and plasma in man and animals. CRC Crit. Reviews Toxicol. March, 1972: 153-202.

Worthing, C.R. and S.B. Walker, Ed. 1983. The Pesticide Manual, 7th ed. British Crop Protection Council, The Lavenham Press Ltd., Suffolk, England. p. 130.

APPENDIX

LITERATURE SEARCHED

This profile is based on data identified by computerized literature searches of:

CASR online (U.S. EPA Chemical Activities Status Report)
CAS online STN Internation
TOXLINE
TOXBACK 76
TOXBACK 65
RTECS
OHM TADS
STORET
SRC Environmental Fate Data Bases
SANSS
AQUIRE
TSCAPP

These searches were conducted in August, 1985. In addition, hand searches were made of Chemical Abstracts (Collective Indices 6 and 7), and the following secondary sources were reviewed:

ACGIH (American Conference of Governmental Industrial Hygienists). 1980. Documentation of the Threshold Limit Values, 4th ed. (Includes Supplemental Documentation through 1984). Cincinnati, OH. 486 p.

ACGIH (American Conference of Governmental Industrial Hygienists). 1985. TLVs: Threshold Limit Values for Chemical Substances and Physical Agents in the Workroom Environment with Intended Changes for 1985-1986. Cincinnati, OH. 114 p.

Clayton, G.D. and F.E. Clayton, Ed. 1981. Patty's Industrial Hygiene and Toxicology, 3rd rev. ed., Vol. 2A. John Wiley and Sons, NY. p. 2878.

Clayton, G.D. and F.E. Clayton, Ed. 1981. Patty's Industrial Hygiene and Toxicology, 3rd rev. ed., Vol. 2B. John Wiley and Sons, NY. p. 2879-3816.

Clayton, G.D. and F.E. Clayton, Ed. 1982. Patty's Industrial Hygiene and Toxicology, 3rd rev. ed., Vol. 2C. John Wiley and Sons, NY. p. 3817-5112.

Grayson, M. and D. Eckroth, Ed. 1978-1984. Kirk-Othmer Encyclopedia of Chemical Technology, 3rd ed. John Wiley and Sons, NY. 24 Volumes and Supplement.

Hamilton, A. and H.L. Hardy. 1974. Industrial Toxicology, 3rd ed. Publishing Sciences Group, Inc., MA. 575 p.

IARC (International Agency for Research on Cancer). IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Humans. WHO, IARC, Lyons, France.

ITII (International Technology Information Institute). 1982. Toxic and Hazardous Industrial Chemicals Safety Manual for Handling and Disposal with Toxicity and Hazard Data. ITII, Tokyo, Japan. 700 p.

NTP (National Toxicology Program). 1985. Toxicology Research and Testing Program. Chemicals on Standard Protocol. Management Status.

Ouellette, R.P. and J.A. King. 1977. Chemical Week Pesticide Register. McGraw-Hill Book Co., NY.

Sax, I.N. 1984. Dangerous Properties of Industrial Materials, 6th ed. Van Nostrand Reinhold Co., NY.

SRI (Stanford Research Institute). 1985. Directory of Chemical Producers. Menlo Park, CA.

U.S. EPA. 1985. Status Report on Rebuttable Presumption Against Registration (RPAR) or Special Review Process. Registration Standards and the Data Call in Programs. Office of Pesticide Programs, Washington, DC.

U.S. EPA. 1985. CSB Existing Chemical Assessment Tracking System. Name and CAS Number Ordered Indexes. Office of Toxic Substances, Washington, DC.

USITC (U.S. International Trade Commission). 1983. Synthetic Organic Chemicals. U.S. Production and Sales, 1982, USITC Publ. 1422. Washington, DC.

Verschueren, K. 1983. Handbook of Environmental Data on Organic Chemicals, 2nd ed. Van Nostrand Reinhold Co., NY.

Worthing, C.R. and S.B. Walker, Ed. 1983. The Pesticide Manual. British Crop Protection Council. 695 p.

Windholz, M., Ed. 1983. The Merck Index, 10th ed. Merck and Co., Inc., Rahway, NJ.

In addition, approximately 30 compendia of aquatic toxicity data were reviewed, including the following:

Battelle's Columbus Laboratories. 1971. Water Quality Criteria Data Book. Volume 3. Effects of Chemicals on Aquatic Life. Selected Data from the Literature through 1968. Prepared for the U.S. EPA under contract No. 68-01-0007. Washington, DC.

Johnson, W.W. and M.T. Finley. 1980. Handbook of Acute Toxicity of Chemicals to Fish and Aquatic Invertebrates. Summaries of Toxicity Tests Conducted at Columbia National Fisheries Research Laboratory. 1965-1978. U.S. Dept. Interior, Fish and Wildlife Service Resource Publ. 137. Washington, DC.

McKee, J.E. and H.W. Wolf. 1963. Water Quality Criteria, 2nd ed. Prepared for the Resources Agency of California. State Water Quality Control Board. Publ. No. 3-A.

Pimental, D. 1971. Ecological Effect of Pesticides on Non-Target Species. PB-269605. Prepared for the U.S. EPA, Washington, DC.

Schneider, B.A. 1979. Toxicology Handbook. Mammalian and Aquatic Data. Book 1: Toxicology Data. EPA 540/9-79-003. NTIS PB 80-196876. Office of Pesticide Programs, U.S. EPA, Washington, DC.